

**REMARKS**

Claims 17-21 are currently pending. By the present communication, no claims have been amended, added or canceled. Accordingly, upon entry of this amendment claims 17-21 will remain pending.

**Rejection under 35 U.S.C. §103**

Applicants respectfully traverse the rejection of claims 17-21 under 35 U.S.C. §103(a) as allegedly being unpatentable over Magai et al. (EP Appln. No. EP 0 864 645 A1; hereinafter, “Magai”) in view of Zhang et al. (BBRC 227:707-11, 1996; hereinafter, “Zhang”) or Nabel et al. (U.S. Patent No. 5,733,543; hereinafter, “Nabel”). The recent U.S. Supreme Court decision in KSR International v. Teleflex Inc. (82 USPQ2d 1385), modified the standard for establishing a *prima facie* case of obviousness. Under the KSR rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

Applicants traverse the rejection for at least the reasons already of record and those that follow. In particular, Applicants maintain that it is not clear how one of skill in the art, in view of Magai, would have understood that the host cells comprising a non-segmented (-)RNA virus lacking the M gene, thus rendering it incapable of forming infectious particles, would still be able to expand the transgene from an infected cell to a neighboring cell via cell-to-cell contact. Indeed, as previously argued, Magai is absolutely silent with regard any disclosure that cells comprising Sendai virus lacking a gene encoding M protein are capable of introducing the transgene to a neighboring cell by contact infiltration. Moreover, Zhang and Nabel, which are equally silent with regard to any disclosure or suggestion that a non-segmented (-)RNA virus lacking a gene encoding M protein or comprises an inactivated gene encoding M protein is capable of transferring its genome by contact infiltration, fail to cure the deficiencies of Magai.

Accordingly, the skilled artisan would have no motivation to combine the references nor would the artisan have a reasonable expectation of achieving the present methods in view of the references.

While the Office Action acknowledges that Magai is silent with regard to transfer of Sendai viral genes into neighboring cells by contact infiltration, the Action alleges that,

[t]he Sendai viral RNA (and transgene) would be expected to be transferred to neighboring cells by contact infiltration because the F and HN proteins of the Sendai virus are expressed in the host cells by the viral constructs disclosed by applicants and Magai et al.

(Office Action at page 4, lines 14-17). However, contrary to the allegation as set forth in the Action, it is unclear how the skilled artisan could expect the transfer of Sendai virus based on this cited passage and the further teachings of Magai.

Magai further teaches that “M, F and HN are components necessary for constructing the viral structure.” (Magai, page 5, line 34 of EP 0 864 645 A1) and that “‘the gene related to the disseminative capability’ refers to any one of the M, F and HN genes” (Magai, page 8, line 39). However, Magai fails to disclose a role for M, F or HN proteins in viral budding or cell fusion. Thus, it is unclear how, absent the present disclosure, the skilled artisan would have reasonably expected an M protein deficient Sendai viral RNA to be transferred to neighboring cells.

It is respectfully submitted that prior to the present disclosure, contact infiltration caused by Sendai virus lacking an M gene was not known. Indeed, the Examiner appears to base the above assertion on Applicants’ own disclosure, citing paragraph [0072].

Indeed, with regard to the mechanism by which the viral RNA is introduced into neighboring cells by contact infiltration, applicants themselves, in specification paragraph [0072], indicate that: “[T]his mode of propagation is probably due to cell fusion mediated by F and HN proteins. Namely, among proteins encoded by Sendai virus, F and HN proteins are expressed as a membrane protein on the cell surface, and M protein supports F and HN proteins as an intracellular anchor in virus budding.. In case of the M deletion type and M defect type, budding does not occur because the anchor is lost. However, F and HN proteins are expressed on the cell surface, and cell fusion occurs mediated by these proteins, so that virus genome can be transferred into surrounding cells. In this way, it is possible to realize virus propagation without budding (Figure 9)[”]

(Office Action at page 4, line 17 to page 5, line 2). Applicants respectfully point out that the analysis provided at paragraph [0072] of the present specification was performed subsequent to the publication of Magai. In particular, the present inventors revealed that the Sendai virus lacking an M gene cannot produce infective particles but can, however, spread via cell-to-cell contact and can generate viral plaques. Based on this observation, the inventors hypothesized that the underlying mechanism was as described in paragraph [0072]. Such a mechanism for spreading of Sendai virus was unknown prior to the present disclosure.

Therefore, in the absence of the present disclosure (which demonstrates that Sendai virus lacking the M gene can be transferred to another cell via contact infiltration), one of skill in the art could not have predicted the spread of Sendai virus in the absence of viral budding. Applicants submit that it is axiomatic that one cannot simply use the Applicants' disclosure as a "blueprint" to reconstruct, by hindsight, Applicants' claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Since there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

To the extent that the Examiner is arguing that the spreading of the Sendai virus via contact infiltration is an inherent property, asserting that "because the mechanism of fusion of neighboring cells with cells expressing the Sendai viral F and HN proteins is an inherent biological process which would occur whether or not it is explicitly recited in the reference" (page 5, lines 9-14 of the Office Action), Applicants respectfully submit that such reasoning is not proper. Indeed, according to the Federal Circuit, "[o]bviousness cannot be predicated on what is unknown." In re Spormann, 363 F.2d 444, 448, 150 USPQ 449, 452 (CCPA 1966). Such a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection. See In re Newell, 891 F.2d 899, 901, 13 USPQ2d 1248, 1250 (Fed. Cir. 1989)." (In re Rijckaert, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993)).

In summary, Applicants respectfully submit that Magai is absolutely silent with regard to the suggestion that a non-segmented (-)RNA virus, which lacks a gene encoding M protein or comprises an inactivated gene encoding M protein and is therefore incapable of transferring its

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genome by infectious particles, is capable of transferring its genome by contact infiltration. Applicants further submit that because both Zhang and Nabel are equally silent with regard to suggesting that a non-segmented (-)RNA virus which lacks a gene encoding M protein is capable of transferring its genome by contact infiltration, neither reference cures the deficiencies of Magai. Accordingly, the skilled artisan would have no motivation to combine the references nor would the artisan have a reasonable expectation of achieving the present methods in view of the references. Thus, the Action has not established a case *prima facie* obviousness of the invention over Magai, Zhang, or Nable, either alone or in combination. Withdrawal of the rejection is respectfully requested.

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## CONCLUSION

In summary, for the reasons set forth herein, Applicants respectfully submit that the claims clearly and patentably define the invention, and allowance of the claims is respectfully requested. If the Examiner would like to discuss any issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

The Commissioner is hereby authorized to charge \$525.00 as payment for the Petition for a Three-Month Extension of Time fee to Deposit Account No. 07-1896. Additionally, the Commissioner is hereby authorized to charge any other fees that may be due in connection with the filing of this paper, or credit any overpayment to Deposit Account No. 07-1896, referencing the above-identified docket number.

Respectfully submitted,

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